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Total Number of Pages in This Submission: 37

Application Number	10/643,797
Filing Date	08/19/2003
First Named Inventor	Richard G. Langlois
Art Unit	1641
Examiner Name	Yang, Nelson C
Attorney Docket Number	IL-11052

ENCLOSURES (*Check all that apply*)

- ☐ Fee Transmittal Form
- ☐ Fee Attached
- ☐ Amendment/Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
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- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
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  - ☐ Reply to Missing Parts under 37 CFR 1.52 or 1.53
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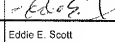
Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Lawrence Livermore National Security, LLC		
Signature			
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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant :	Richard G. Langlois et al.	Docket No. :	IL-11052
Serial No. :	10/643,797	Art Unit :	1641
Filed :	08/19/2003	Examiner :	Nelson C. Yang
For :	SYSTEM FOR AUTONOMOUS MONITORING OF BIOAGENTS		

Honorable Commissioner for Patents
Alexandria, VA 22313-1450

Attention: Board of Patent Appeals and Interferences

Dear Sir:

APPELLANTS' BRIEF (37 C.F.R. § 1.192)

This brief is submitted in support of Appellants' notice of appeal from the decision of the Examiner, mailed September 4, 2007 finally rejecting claims 1-5, 12, 15-16, 19, 27, 29, and 31-40 of the subject application.

Appellants' notice of appeal was mailed November 26, 2007.

One copy of the brief is being transmitted per 37 C.F.R. § 41.37.

TABLE OF CONTENTS

I. REAL PARTY IN INTEREST

The real party in interest is:

Lawrence Livermore National Security, LLC and the United States of America as represented by the United States Department of Energy (DOE) by virtue of an assignment by the inventor as duly recorded in the Assignment Branch of the U.S. Patent and Trademark Office.

II. RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

III. STATUS OF CLAIMS

The application as originally filed contained claims 1-50.

The claims on appeal are claims 1-5, 12, 15-16, 19, 27, 29, and 31-40.

The status of all the claims in the proceeding (*e.g.*, rejected, allowed or confirmed, withdrawn, objected to, canceled) is:

Claims 41-50 are withdrawn from consideration.

Claims 6-11, 13-14, 17-18, 20-26, 28, and 30 are cancelled.

Claims 1-5, 12, 15-16, 19, 27, 29, and 31-40 are rejected.

Claims 1-5, 12, 15-16, 19, 27, 29, and 31-40 on appeal are reproduced in the Appendix.

IV. STATUS OF AMENDMENTS

There have been no amendments filed subsequent to the Final Rejection mailed September 4, 2007.

V. SUMMARY OF CLAIMED SUBJECT MATTER

Appellants' invention provides a system for monitoring air for bioagents. Portions of Appellants' specification are quoted and the quote is identified by the page and line numbers.

At present there are more than 30 pathogens and toxins on various agency threat lists. Public health personnel rarely see most of the pathogens so they have difficulty identifying them quickly. In addition, many pathogenic infections aren't immediately symptomatic, with delays as long as several days, limiting options to control the disease and treat the patients. The lack of a practical monitoring network capable of rapidly detecting and identifying multiple pathogens or toxins on current threat lists translates into a major deficiency in the United States ability to counter biological terrorism. (Page 11, lines 18-19 and Page 12, lines 1-6)

In Appellants' invention particles in the air are separated by size and the particles of a size range that are likely to contain the bioagents are collected. Any bioagents in the collected particles are detected by a detector system. (Page 6, lines 7-10) Appellants' invention is illustrated in FIGS. 6, 11, 13, below.

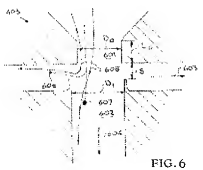
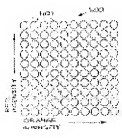


FIG. 6



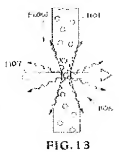


FIG. 13

Small diameter polystyrene beads are coded with 1000s of antibodies. The sample is first exposed to the beads and the bioagent, if present, is bound to the

bead. A second, fluorescently labeled antibody is then added to the sample resulting in a highly fluorescent target for flow analysis. Since the assay is performed on a microbead matrix, it is possible to measure all types of pathogens, including viruses and toxins. Each microbead is colored with a unique combination of red and orange emitting dyes. The number of agents that can be detected from a single sample is limited only by the number of colored bead sets. The system includes the following components: microbead specific reagents, incubation/mixing chambers, a microbead capture array, and an optical measurement and decoding system. (Page 41, lines 17-19 and Page 41, lines 1-8)

There exists a critical need to develop distributed biothreat agent sensor networks that can operate in civilian applications. To operate in "Detect to Protect/Warn" type detection architectures, these platforms need to have several key properties. They need to be capable of detecting pathogens within a 1-2 hour time window, allowing for enough time to respond to an event. They need to be extremely low cost to maintain, since continuous monitoring is essential for many applications. These platforms need to have sufficient sensitivity to cover a broad geographical area (limiting the necessary number of sensors) and have sufficient selectivity to virtually eliminate false positives. (Page 1, lines 17-19 and Page 2, lines 1-9)

Applicants' invention provides an Autonomous Pathogen Detection System (APDS) for monitoring the environment to protect the public from the release of hazardous biological agents. The Autonomous Pathogen Detection System is a countermeasure to bioterrorism, one of the most serious threats to the safety of United States citizens, citizens of other countries, and the military. There is one (1) independent claim, claim 1, involved in the appeal. Appellants' independent claim involved in the appeal is "read on" Appellants' original specification.

Claim 1	Specification & Drawings
1. An autonomous monitoring apparatus for monitoring air for bioagents wherein the air may contain potential bioagent particles, comprising:	The present invention provides a system for monitoring air for bioagents. Particles in the air are separated by size and the particles of a size range that are likely to contain the bioagents are collected. (Page 6, lines 7-9)
a collector for gathering said air being monitored, said collector separating selected potential bioagent particles from said air;	an aerosol collector system continuously samples the air and traps particles in a swirling buffer solution. Particles of a given size distribution are selected by varying the flow rate across a virtual impactor unit. (Page 21, lines 5-8)
a wetted wall sample preparer for preparing a sample of said selected potential bioagent particles, said wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector wherein said wetted wall sample preparer includes a wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid and a unit for adding optically encoded microbeads imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen to said liquid and said selected potential bioagent particles; and	... the collector includes a wetted-wall cyclone collector that receives product air flow and traps and concentrates potential bioagent particles of a predetermined particle size range in a liquid. (Page 7, lines 13-15) The beads are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of one hundred beads, each with a unique spectral address. Each bead 1101 is coated with capture antibodies specific for a given antigen as illustrated in FIG. 12. (Page 44, lines 11-14)
a detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads and	A detector for detecting the bioagents in the sample is operatively connected to the sample preparation means. (Page 6, lines 18-19)

Claim 1 (Continued)	Specification & Drawings
wherein said detector includes a flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents.	The APDS 300 integrates a flow cytometer and PCR detector (Page 19, line 5) Each optically encoded and fluorescently labeled microbead is individually read in a flow cytometer, and fluorescent intensities are then correlated with bioagent concentrations. (Page 19, line 5)

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The Final Rejection mailed September 4, 2007 states three grounds of rejection. The three grounds of rejection are summarized as follows:

Grounds of Rejection #1 - Claims 1-4, 12, 27, 29, 31-35, 40 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Miles et al US 6,576,459 (hereinafter Miles) in view of Casey et al US 2002/0187470 (hereinafter Casey) and in view of Lawless et al US 4,923,491 (hereinafter Lawless). The rejection is stated in numbered paragraph 1 on page 2 of the Final Rejection mailed September 4, 2007.

Grounds of Rejection #2 - Claims 1, 15-16, 19, 33, 36-39 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Colston, Jr. et al US 200310032172 (hereinafter Colston) in view of Casey et al US 2002/0187470 (hereinafter Casey) and in view of Lawless et al [S 4,923,491 (hereinafter Lawless). The rejection is stated in numbered paragraph 9 on page 5 of the Final Rejection mailed September 4, 2007.

Grounds of Rejection #3 - Claims 1-5, 32, 33, 35-37 were rejected are rejected under 35 U.S.C. § 103(a) as being unpatentable over Daugherty et al US 2004/0028561 (hereinafter Daugherty) in view of Casey et al US 2002/0187470 (hereinafter Casey). The rejection is stated in numbered paragraph 17 on page 8 of the Final Rejection mailed September 4, 2007.

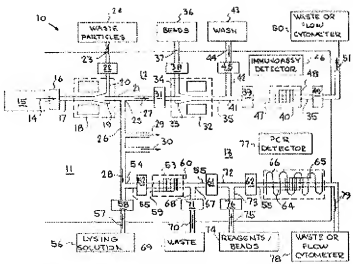
VII. ARGUMENT

Argument Relating to Grounds of Rejection #1

The rejection of Appellants' claims 1-4, 12, 27, 29, 31-35, 40 as being obvious over Miles in view of Casey and in view of Lawless does not meet the standard of 35 U.S.C. § 103(a).

The Miles Reference

The Miles reference is United States Patent No. 6,576,459 for a sample preparation and detection device for infectious agents illustrated in the figure and portion of specification of the patent reproduced below.



"The sample preparation and detection device comprises a system or device generally indication at 10 located on a single compact, field-portable microchip 11 and includes an immunoassay section 12 and a PCR assay section 13. Sample containing pathogenic particles indicated by arrow 14 is moved from a collector or other source 15 by an MHD pump 16 through a microchannel 17 into an ultrasonic fractionation or filtering assembly generally indicated at 18 and which is sensitive to density and size differences between particles. Microchannel 17 terminates in a separator 19 with microchannels 20 and 21 extending from separator 19. Microchannel 20 is directed through a MHD pump 22 and carries large particles and dense particles indicated by arrow 23, which are transferred to waste as indicated at 24. Microchannel 21 includes a function 25 from which extends a microchannel 26, with microchannel 21 supplying sample to immunoassay section 12 as indicated by arrow 27 and microchannel 26 supplying sample to PCR assay section 13 for DNA analysis, as indicated by arrow 28."

Appellants Disagree with Examiner's Finding of Fact – Miles Reference

The Appellants disagree with the Examiner's Finding of Fact regarding the Miles reference. The Final Rejection mailed September 4, 2007 states: "Miles et al fail to teach that the use of optically encoded microbeads imbedded with

precise ratios of red and orange fluorescent dyes yielding an array of beads, each with a unique spectral address and coated with capture antibodies specific for a given antigen, and also fails to teach an aerosol collector that is a wetted wall cyclone collector that concentrates said potential bioagent particles in a liquid."

Appellants point out that there are other claim limitations that are not taught by the Miles reference. The Miles reference does not show Appellants' "autonomous monitoring apparatus for monitoring air for bioagents wherein the air may contain potential bioagent particles." The Miles reference only shows a "sample preparation and detection device comprises a system or device generally indication at 10 located on a single compact, field-portable microchip." The Miles reference does not show an autonomous monitoring apparatus for monitoring air for bioagents.

The Miles reference does not show Appellants' "collector for gathering said air being monitored, said collector separating selected potential bioagent particles from said air." The Miles reference only shows a "collector or other source 15." The Miles reference does not show a collector separating selected potential bioagent particles from air.

The Miles reference does not show Appellants' "wetted wall sample preparer for preparing a sample of said selected potential bioagent particles, said wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector wherein said wetted wall sample preparer includes a wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid." The Miles reference only shows a "collector or other source 15." The Miles reference does not show a "wetted wall sample preparer" or a "wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample

from said air gathered by said collector" or a "wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid."

The Miles reference does not show Appellants' "detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads." The Miles reference only shows "immunoassay detector 46" and "PCR detector 77." The Miles reference does not show a detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads.

The Miles reference does not show Appellants' "flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents." The Miles reference only shows a "immunoassay detector 46" and "PCR detector 77." The Miles reference does not show a flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents.

The Casey et al Reference

The Casey et al reference is United States Published Patent Application No. 2002/0187470 disclosing methods for rapid detection of single nucleotide polymorphisms (SNPs) in a nucleic acid sample. For example, the Casey et al reference discloses the following method:

"a method of determining a selected nucleotide polymorphism in genomic DNA treated to reduce viscosity comprising (a) performing an amplification of the genomic DNA using a first nucleic acid primer comprising a region complementary to a section of one strand of the nucleic acid that is 5' of the selected nucleotide, and a second nucleic acid primer complimentary to a section of the opposite strand of the nucleic acid downstream of the selected nucleotide, under conditions for specific amplification of the region of the selected nucleotide between the two primers, to form a PCR product; (b) contacting the PCR product with a first nucleic acid linked at its 5' end to a detectably tagged mobile solid support, wherein the first nucleic acid comprises a region complementary to a section of one strand of the PCR product that is directly 5' of and adjacent to the selected nucleotide, under hybridization conditions to form a hybridization product; (c) performing a primer extension reaction with the hybridization product and a detectably labeled, identified chain-terminating nucleotide under conditions for primer extension; (d) detecting the presence or absence of a label incorporated into the hybridization product, the presence of a label indicating the incorporation of the labeled chain-terminating nucleotide into the hybridization product, and the identity of the incorporated labeled chain-terminating nucleotide indicating the identity of the nucleotide complementary to the selected nucleotide; and (e) comparing the identity of the selected nucleotide with a non-polymorphic nucleotide, a different identity of the selected nucleotide from that of the non-polymorphic nucleotide indicating a polymorphism of that selected nucleotide."

The Lawless et al Reference

The Lawless et al reference is United States Patent No. 4,923,491 for a centrifugal filter for separating aerosol particles from a gas stream illustrated in FIG. 5 and the abstract reproduced below.

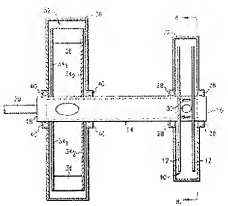


FIG. 6

A centrifugal filter for separating aerosol particles from a gas stream including a rotatable hollow hub and at least one pair of disks fixedly mounted in spaced

apart relationship on the hub within a stationary housing mounted on the hub. The hub is perforated in the region between the two disks and is coupled to a vacuum pump so that the interior of the hub is at a lower pressure relative to the space between the disks. The hub is rotated, causing rotation of the disks. Aerosol particles in a flow gas are introduced between the disks and the housing at the periphery of the rotating disks. The pressure differential produced at the hub perforations draws the aerosol laden gas toward the hub. As the aerosol laden gas enters between the rotating disks and the housing, it experiences an acceleration to nearly the angular velocity of the disks, which results in a centrifugal force being applied to the aerosol particles in a direction opposite to the drag force exerted by the vacuum pump. The particles in the gas stream remain entrained in the outer periphery where they are removed, while the gas continues its motion toward the hub, thereby effecting separation.

The Final Rejection Does Not Establish a *Prima Facie* Case of Obviousness

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966) that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) include, "Ascertaining the differences between the prior art and the claims at issue." The Examiner bears the initial burden of factually supporting a *prima facie* conclusion of obviousness (M.P.E.P. Section 2142). Three basic criteria must be met in order for the Examiner to establish a *prima facie* case of obviousness. The prior art reference (or reference when combined) must teach or suggest all the claim limitations. There must be a reasonable expectation of success with the proposed combination. The Examiner must follow the "Examination Guidelines for Determining Obviousness in Light of the Supreme Court's KSR v. Teleflex Decision" published October 10, 2007. These guidelines include the requirement that the Examiner provide reasons for combining the references to produce the proposed combination.

Miles, Casey, and Lawless Do Not Teach All Claim Limitations

The Miles, Casey, and Lawless references do not disclose a number of Applicants' claim limitations. The criteria that the prior art reference, or

references when combined, must teach or suggest all the claim limitations has not been met. The Miles reference and the Casey reference and the Lawless reference do not disclose the limitations of Applicants' claims 1-4, 12, 27, 29, 31-35, 40 identified below.

"autonomous monitoring apparatus for monitoring air for bioagents wherein the air may contain potential bioagent particles," or

"a collector for gathering said air being monitored, said collector separating selected potential bioagent particles from said air," or

"a wetted wall sample preparer for preparing a sample of said selected potential bioagent particles, said wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector wherein said wetted wall sample preparer includes a wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid and a unit for adding optically encoded microbeads imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen to said liquid and said selected potential bioagent particles," or

"a detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads," or

"wherein said detector includes a flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents," or

"said collector includes a separator for separating said potential bioagent particles from said other particles," or

"means for lysis of said spores," or

"polystyrene beads," or

"said laser unit includes a red laser that classifies said microbeads and a green laser that quantifies said microbeads," or

"said sample preparation means includes optically encoded microbeads and bead suspension/mixer means for suspending said microbeads for a predetermined time period."

Since the limitations listed and described above are not shown by the Miles reference, the Casey reference, or the Lawless reference, a *prima facie* case of obviousness has not been established. Further, since the Miles reference and the Casey reference and the Lawless reference fail to show the claim limitations of Applicants' claims 1-4, 12, 27, 29, 31-35, 40 there can be no combination of the three references that would show Applicant's invention. There is no combination of the Miles reference and the Casey reference and the Lawless reference that would produce the combination of elements of Applicants' claims 1-4, 12, 27, 29, 31-35, 40. Thus, the combination of references in the Office Action mailed September 4, 2007 fails to support a rejection of claims 1-4, 12, 27, 29, 31-35, 40 under 35 U.S.C. § 103(a), and the rejection should be reversed.

No Reasons for Combining Miles, Casey, and the Lawless

The criteria that the Examiner must provide reasons for combining the references has not been established. The Examiner must follow the "Examination Guidelines for Determining Obviousness in Light of the Supreme Court's KSR v. Teleflex Decision" published October 10, 2007. These guidelines include the requirement that the Examiner provide reasons for combining the references to produce the proposed combination.

The rejection in the Office Action mailed September 4, 2007 does not provide an explanation of how or why the Miles reference and the Casey reference and the Lawless reference would be combined. The Miles reference and the Casey reference and the Lawless reference do not recognize the problem solved by Applicant's claimed invention. The Miles reference and the Casey

reference and the Lawless reference fail to disclose the benefits of Applicants claimed invention wherein "particles in the air are separated by size and the particles of a size range that are likely to contain the bioagents are collected and any bioagents in the collected particles are detected by a detector." Thus, the combination of references in the Office Action mailed September 4, 2007 fails to support a rejection of claims 1-4, 12, 27, 29, 31-35, 40 under 35 U.S.C. § 103(a), and the rejection should be reversed.

Argument Relating to Grounds of Rejection #2

The rejection of Appellants' claims 1, 15-16, 19, 33, 36-39 as being obvious over Colston in view of Casey and in view of Lawless does not meet the standard of 35 U.S.C. § 103(a).

The Colston et al Reference

The Colston et al reference is United States Published Patent Application No. 2003/0032172 for an automated nucleic acid assay system illustrated in figure 2 and the portion of specification of the patent reproduced below.

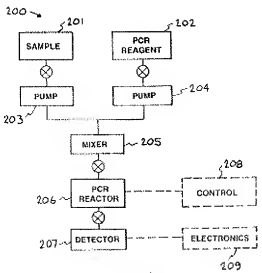


FIG. 2

"The system 200 provides a system capable of performing, singly or in combination, sample preparation, nucleic acid amplification, and nucleic acid detection functions. The nucleic acid assay system 200 includes a number components. A sample is contained in unit 201. A PCR reagent is contained in unit 202. A pump 203 transfers the sample from unit 201 into mixer 205. A pump 204 transfers the PCR reagent from unit 202 into mixer 205. The mixer 205 combines the sample and the PCR reagent. In one embodiment the PCR reagent includes primers. In another embodiment the PCR reagent includes oligos. The mixer 205 can be, for example, a super serpentine reactor, available from Global FIA, Inc, Fox Island, Wash. The mixed sample and reagent are transferred to a PCR reactor 206. This results in an amplified sample. In one embodiment the PCR reactor 206 includes an embedded thermocouple calibration conduit. PCR amplification devices are described in publications such as U.S. Pat. No. 5,589,136 for silicon-based sleeve devices for chemical reactions, assigned to the Regents of the University of California, inventors: M. Allen Northrup, Raymond P. Mariella, Jr., Anthony V. Carrano, and Joseph W. Balch, patented Dec. 31, 1996 and many are commercially available such as ABI PRISM® 7700 Sequence Detection System by Applied Biosystems; iCycler iQ Real-Time PCR Detection System by Bio-Rad; and Smart Cycler® System by Cepheid. The amplified sample is transferred from the PCR reactor 206 detector 207. The detector can be, for example, a detection system described in publications and products produced by Cepheid and Baltimore-based Environmental Technologies Group, Inc. (ETG), a part of London-based Smiths Aerospace."

Appellants Disagree with Examiner's Finding of Fact – Colston Reference

The Appellants disagree with the Examiner's Finding of Fact regarding the Colston reference. The Final Rejection mailed September 4, 2007 states: "Colston et al fail to teach that the use of optically encoded microbeads imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads, each with a unique spectral address and coated with capture antibodies specific for a given antigen, and also fails to teach an aerosol collector that is a wetted wall cyclone collector that concentrates said potential bioagent particles in a liquid."

Appellants point out that there are other claim limitations that are not taught by the Colston reference. The Colston reference does not show Appellants' "collector for gathering said air being monitored, said collector

separating selected potential bioagent particles from said air." The Colston reference only shows "means for holding a sample." The Colston reference does not show a collector separating selected potential bioagent particles from air.

The Colston reference does not show Appellants' "wetted wall sample preparer for preparing a sample of said selected potential bioagent particles, said wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector wherein said wetted wall sample preparer includes a wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid." The Colston reference does not show a "wetted wall sample preparer" or a "wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector" or a "wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid."

The Colston reference does not show Appellants' "detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads." The Colston reference does not show a detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads.

The Colston reference does not show Appellants' "flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents." The Colston reference does

not show a flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents.

The Casey et al Reference

The Casey et al reference is United States Published Patent Application No. 2002/0187470 disclosing methods for rapid detection of single nucleotide polymorphisms (SNPs) in a nucleic acid sample. For example, the Casey et al reference discloses the following method:

> "a method of determining a selected nucleotide polymorphism in genomic DNA treated to reduce viscosity comprising (a) performing an amplification of the genomic DNA using a first nucleic acid primer comprising a region complementary to a section of one strand of the nucleic acid that is 5' of the selected nucleotide, and a second nucleic acid primer complimentary to a section of the opposite strand of the nucleic acid downstream of the selected nucleotide, under conditions for specific amplification of the region of the selected nucleotide between the two primers, to form a PCR product; (b) contacting the PCR product with a first nucleic acid linked at its 5' end to a detectably tagged mobile solid support, wherein the first nucleic acid comprises a region complementary to a section of one strand of the PCR product that is directly 5' of and adjacent to the selected nucleotide, under hybridization conditions to form a hybridization product; (c) performing a primer extension reaction with the hybridization product and a detectably labeled, identified chain-terminating nucleotide under conditions for primer extension; (d) detecting the presence or absence of a label incorporated into the hybridization product, the presence of a label indicating the incorporation of the labeled chain-terminating nucleotide into the hybridization product, and the identity of the incorporated labeled chain-terminating nucleotide indicating the identity of the nucleotide complementary to the selected nucleotide; and (e) comparing the identity of the selected nucleotide with a non-polymorphic nucleotide, a different identity of the selected nucleotide from that of the non-polymorphic nucleotide indicating a polymorphism of that selected nucleotide."

The Lawless et al Reference

The Lawless et al reference is United States Patent No. 4,923,491 for a centrifugal filter for separating aerosol particles from a gas stream illustrated in FIG. 5 and the abstract reproduced below.

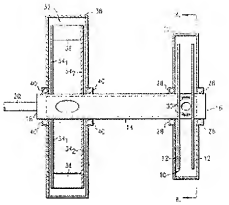


FIG. 6

A centrifugal filter for separating aerosol particles from a gas stream including a rotatable hollow hub and at least one pair of disks fixedly mounted in spaced apart relationship on the hub within a stationary housing mounted on the hub. The hub is perforated in the region between the two disks and is coupled to a vacuum pump so that the interior of the hub is at a lower pressure relative to the space between the disks. The hub is rotated, causing rotation of the disks. Aerosol particles in a flow gas are introduced between the disks and the housing at the periphery of the rotating disks. The pressure differential produced at the hub perforations draws the aerosol laden gas toward the hub. As the aerosol laden gas enters between the rotating disks and the housing, it experiences an acceleration to nearly the angular velocity of the disks, which results in a centrifugal force being applied to the aerosol particles in a direction opposite to the drag force exerted by the vacuum pump. The particles in the gas stream remain entrained in the outer periphery where they are removed, while the gas continues its motion toward the hub, thereby effecting separation.

The Final Rejection Does Not Establish a *Prima Facie* Case of Obviousness

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966) that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) include, "Ascertaining the differences between the prior art and the claims at issue." The Examiner bears the initial

burden of factually supporting a *prima facie* conclusion of obviousness (M.P.E.P. Section 2142). Three basic criteria must be met in order for the Examiner to establish a *prima facie* case of obviousness. The prior art reference (or reference when combined) must teach or suggest all the claim limitations. There must be a reasonable expectation of success with the proposed combination. The Examiner must follow the "Examination Guidelines for Determining Obviousness in Light of the Supreme Court's KSR v. Teleflex Decision" published October 10, 2007. These guidelines include the requirement that the Examiner provide reasons for combining the references to produce the proposed combination.

Colston, Casey, and Lawless Do Not Teach All Claim Limitations

The Colston, Casey, and Lawless references do not disclose a number of Applicants' claim limitations. The criteria that the prior art reference, or references when combined, must teach or suggest all the claim limitations has not been met. The Colston reference and the Casey reference and the Lawless reference do not disclose the limitations of Applicants' claims 1, 15-16, 19, 33, 36-39 identified below.

"a collector for gathering said air being monitored, said collector separating selected potential bioagent particles from said air," or

"a wetted wall sample preparer for preparing a sample of said selected potential bioagent particles, said wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector wherein said wetted wall sample preparer includes a wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid and a unit for adding optically encoded microbeads imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen to said liquid and said selected potential bioagent particles," or

"a detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads," or

"wherein said detector includes a flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents," or

"a sequential injection analysis system," or

"said wetted wall sample preparer includes a flow injection analysis system," or

"a super serpentine reactor," or

"confirmation means for confirming said bioagents in said sample," or

"said confirmation means is a real time PCR detector," or

"said confirmation means includes means for performing PCR amplification," or

"wherein said confirmation means includes means for injecting/aspirating a sample, means for adding PCR reagent, means for mixing sample and reagent, means for transport to PCR reactor, means for performing PCR amplification, means for transport of amplified sample from PCR reactor, and means for detection of PCR amplicon," or

"wherein said confirmation means includes means for injecting/aspirating a sample, means for adding PCR reagent, means for mixing sample and reagent, means for transport to PCR reactor, means for performing PCR amplification, means for transport of amplified sample from PCR reactor, means for detection of PCR amplicon, and means for decontamination and conditioning of all exposed conduits."

Since the limitations listed and described above are not shown by the Colston reference, the Casey reference, or the Lawless reference, a *prima facie* case of obviousness has not been established. Further, since the Colston reference and the Casey reference and the Lawless reference fail to show the claim limitations of Applicants' claims 1, 15-16, 19, 33, 36-39 there can be no combination of the

three references that would show Applicant's invention. There is no combination of the Colston reference and the Casey reference and the Lawless reference that would produce the combination of elements of Applicants' claims 11, 15-16, 19, 33, 36-39. Thus, the combination of references in the Office Action mailed September 4, 2007 fails to support a rejection of claims 1, 15-16, 19, 33, 36-39 under 35 U.S.C. § 103(a), and the rejection should be reversed.

No Reasons for Combining Colston, Casey, and the Lawless

The criteria that the Examiner must provide reasons for combining the references has not been established. The Examiner must follow the "Examination Guidelines for Determining Obviousness in Light of the Supreme Court's KSR v. Teleflex Decision" published October 10, 2007. These guidelines include the requirement that the Examiner provide reasons for combining the references to produce the proposed combination.

The rejection in the Office Action mailed September 4, 2007 does not provide an explanation of how or why the Colston reference and the Casey reference and the Lawless reference would be combined. The Colston reference and the Casey reference and the Lawless reference do not recognize the problem solved by Applicant's claimed invention. The Colston reference and the Casey reference and the Lawless reference fail to disclose the benefits of Applicants claimed invention wherein "particles in the air are separated by size and the particles of a size range that are likely to contain the bioagents are collected and any bioagents in the collected particles are detected by a detector." Thus, the combination of references in the Office Action mailed September 4, 2007 fails to support a rejection of claims 1, 15-16, 19, 33, 36-39 under 35 U.S.C. § 103(a), and the rejection should be reversed.

Argument Relating to Grounds of Rejection #3

The rejection of Appellants' claims 1-5, 32, 33, 35-37 as being obvious over Daugherty in view of Casey does not meet the standard of 35 U.S.C. § 103(a).

The Daugherty Reference

The Daugherty et al reference is United States Published Patent Application No. 2004/0028561 for a system for the detection of pathogens in the mail stream illustrated in figure 6B and the portion of specification of the patent reproduced below.

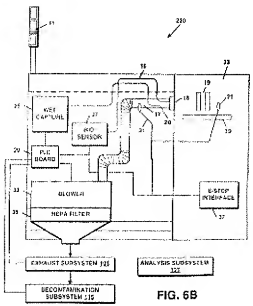


FIG. 6B

"Referring now to FIGS. 6A and 6B, system 220, in which the illustrative embodiment of the control flow 220 for mail sortation is shown. As mail pieces are fed into system 220, through feeder 41, particles are released through normal handling and/or through pinch point pulley assembly 19. Particles are moved through prefilter 18 which allows large particles to pass through the prefilter 18 and exhaust back into the blower/air filtration system 33/35 through simplified hoodless ducting 17 as waste air. Smaller particles enter pitot tube entry 20, into the region in which the particles are tested for contamination. In the illustrative embodiment, the region includes sampling subsystem 123 and triggering subsystem 119 (shown in FIG. 1), embodied in wet capture 25 and biosensor 27/indicator light 11 respectively. After the mail parcels have been fed into the system, they proceed through closed vent/hood 23 on mail transport device 39 towards mail stacker 43 which is enclosed by open vent/hood 45. In general, conventional closed

and open vent/hoods 23 and 45, respectively, are custom-fitted to all types of mail transport equipment (i.e. mail transport equipment manufactured by Lockheed Martin, Pitney-Bowes, Bell & Howell, Siemans, etc.) and conventional mail sortation stacker sections 43, pockets, or sort bin destinations typically installed at mail processing facilities as well as commercial pre-sort facilities and mailrooms."

Appellants Disagree with Examiner's Finding of Fact – Daugherty

The Appellants disagree with the Examiner's Finding of Fact regarding the Daugherty reference. The Final Rejection mailed September 4, 2007 states: "Daugherty et al fail to teach that the use of optically encoded microbeads imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads, each with a unique spectral address and coated with capture antibodies specific for a given antigen, and also fails to teach an aerosol collector that is a wetted wall cyclone collector that concentrates said potential bioagent particles in a liquid."

Appellants point out that there are other claim limitations that are not taught by the Daugherty reference. The Daugherty reference does not show Appellants' "autonomous monitoring apparatus for monitoring air for bioagents wherein the air may contain potential bioagent particles." The Daugherty reference only shows a "system for the detection of pathogens in the mail stream." The Daugherty reference does not show an autonomous monitoring apparatus for monitoring air for bioagents.

The Daugherty reference does not show Appellants' "collector for gathering said air being monitored, said collector separating selected potential bioagent particles from said air." The Daugherty reference only shows a "system for the detection of pathogens in the mail stream." The Daugherty reference does not show a collector separating selected potential bioagent particles from air.

The Daugherty reference does not show Appellants' "wetted wall sample preparer for preparing a sample of said selected potential bioagent particles, said wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector wherein said wetted wall sample preparer includes a wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid." The Daugherty reference only shows a "system for the detection of pathogens in the mail stream." The Daugherty reference does not show a "wetted wall sample preparer" or a "wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector" or a "wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid."

The Daugherty reference does not show Appellants' "detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads." The Daugherty reference only shows "system for the detection of pathogens in the mail stream." The Daugherty reference does not show a detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads.

The Daugherty reference does not show Appellants' "flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents." The Daugherty reference only shows a "system for the detection of pathogens in the mail stream." The

Daugherty reference does not show a flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents.

The Casey et al Reference

The Casey et al reference is United States Published Patent Application No. 2002/0187470 disclosing methods for rapid detection of single nucleotide polymorphisms (SNPs) in a nucleic acid sample. For example, the Casey et al reference discloses the following method:

> "a method of determining a selected nucleotide polymorphism in genomic DNA treated to reduce viscosity comprising (a) performing an amplification of the genomic DNA using a first nucleic acid primer comprising a region complementary to a section of one strand of the nucleic acid that is 5' of the selected nucleotide, and a second nucleic acid primer complimentary to a section of the opposite strand of the nucleic acid downstream of the selected nucleotide, under conditions for specific amplification of the region of the selected nucleotide between the two primers, to form a PCR product; (b) contacting the PCR product with a first nucleic acid linked at its 5' end to a detectably tagged mobile solid support, wherein the first nucleic acid comprises a region complementary to a section of one strand of the PCR product that is directly 5' of and adjacent to the selected nucleotide, under hybridization conditions to form a hybridization product; (c) performing a primer extension reaction with the hybridization product and a detectably labeled, identified chain-terminating nucleotide under conditions for primer extension; (d) detecting the presence or absence of a label incorporated into the hybridization product, the presence of a label indicating the incorporation of the labeled chain-terminating nucleotide into the hybridization product, and the identity of the incorporated labeled chain-terminating nucleotide indicating the identity of the nucleotide complementary to the selected nucleotide; and (e) comparing the identity of the selected nucleotide with a non-polymorphic nucleotide, a different identity of the selected nucleotide from that of the non-polymorphic nucleotide indicating a polymorphism of that selected nucleotide."

The Final Rejection Does Not Establish a *Prima Facie* Case of Obviousness

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966) that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) include, "Ascertaining the differences between the prior art and the claims at issue." The Examiner bears the initial burden of factually supporting a *prima facie* conclusion of obviousness (M.P.E.P. Section 2142). Three basic criteria must be met in order for the Examiner to establish a *prima facie* case of obviousness. The prior art reference (or reference when combined) must teach or suggest all the claim limitations. There must be a reasonable expectation of success with the proposed combination. The Examiner must follow the "Examination Guidelines for Determining Obviousness in Light of the Supreme Court's KSR v. Teleflex Decision" published October 10, 2007. These guidelines include the requirement that the Examiner provide reasons for combining the references to produce the proposed combination.

Daugherty and Casey References Do Not Teach All Claim Limitations

The Daugherty and Casey references do not disclose a number of Applicants' claim limitations. The criteria that the prior art reference, or references when combined, must teach or suggest all the claim limitations has not been met. The Daugherty reference and the Casey reference do not disclose the limitations of Applicants' claims 1-5, 32, 33, 35-37 identified below.

"autonomous monitoring apparatus for monitoring air for bioagents wherein the air may contain potential bioagent particles," or

"a collector for gathering said air being monitored, said collector separating selected potential bioagent particles from said air," or

"a wetted wall sample preparer for preparing a sample of said selected potential bioagent particles, said wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector wherein said wetted wall sample preparer

includes a wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid and a unit for adding optically encoded microbeads imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen to said liquid and said selected potential bioagent particles," or

"a detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads," or

"wherein said detector includes a flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents," or

"wherein said collector is an aerosol collector," or

"said collector includes a separator for separating said potential bioagent particles from said other particles," or

"wherein said collector is an aerosol collector that collects air and includes means for separating said air into a bypass air flow that does not contain said potential bioagent particles of a predetermined particle size range and a product air flow that contains said potential bioagent particles of a predetermined particle size range." Or

"means for lysis of said spores," or

"wherein said confirmation means is a multiplex PCR detector," or

"wherein said confirmation means is a real time PCR detector," or

"wherein said confirmation means includes means for performing PCR amplification."

Since the limitations listed and described above are not shown by the Daugherty reference or the Casey reference, a *prima facie* case of obviousness has not been established. Further, since the Daugherty reference and the Casey

reference fail to show the claim limitations of Applicants' claims 1-5, 32, 33, 35-37 there can be no combination of the two references that would show Applicant's invention. There is no combination of the Daugherty reference and the Casey reference that would produce the combination of elements of Applicants' claims 1-5, 32, 33, 35-37. Thus, the combination of references in the Office Action mailed September 4, 2007 fails to support a rejection of claims 1-5, 32, 33, 35-37 under 35 U.S.C. § 103(a), and the rejection should be reversed.

No Reasons for Combining Daugherty and Casey

The criteria that the Examiner must provide reasons for combining the references has not been established. The Examiner must follow the "Examination Guidelines for Determining Obviousness in Light of the Supreme Court's KSR v. Teleflex Decision" published October 10, 2007. These guidelines include the requirement that the Examiner provide reasons for combining the references to produce the proposed combination.

The rejection in the Office Action mailed September 4, 2007 does not provide an explanation of how or why the Daugherty reference and the Casey reference would be combined. The Daugherty reference and the Casey reference do not recognizes the problem solved by Applicant's claimed invention. The Daugherty reference and the Casey reference fail to disclose the benefits of Applicants claimed invention wherein "particles in the air are separated by size and the particles of a size range that are likely to contain the bioagents are collected and any bioagents in the collected particles are detected by a detector." Thus, the combination of references in the Office Action mailed September 4, 2007 fails to support a rejection of claims 1-5, 32, 33, 35-37 under 35 U.S.C. § 103(a), and the rejection should be reversed.

SUMMARY

The present invention provides an autonomous monitoring apparatus for monitoring air for bioagents. In Appellants' invention bioagents in the collected particles are detected by a detector system. Small diameter polystyrene beads are coded with 1000s of antibodies. The sample is first exposed to the beads and the bioagent, if present, is bound to the bead. A second, fluorescently labeled antibody is then added to the sample resulting in a highly fluorescent target for flow analysis. Each microbead is colored with a unique combination of red and orange emitting dyes. The number of agents that can be detected from a single sample is limited only by the number of colored bead sets. None of the cited references discloses Appellants' claimed invention.

There could be no combination of the references that would support a 35 U. S. C §103(a) rejection of Appellants' claims 1-5, 12, 15-16, 19, 27, 29, and 31-40 and the rejection should be reversed.

It is respectfully requested that claims 1-5, 12, 15-16, 19, 27, 29, and 31-40 on appeal be allowed.

Respectfully submitted,

By: Eddie E. Scott

Eddie E. Scott
Lawrence Livermore National Laboratory
7000 East Avenue, Mail Code L-703
Livermore, CA 94550
Attorney for Appellants
Registration No. 25,220
Telephone No. (925) 424-6897

Date: January 22, 2008

VIII. CLAIMS APPENDIX

1. An autonomous monitoring apparatus for monitoring air for bioagents wherein the air may contain potential bioagent particles, comprising:

a collector for gathering said air being monitored, said collector separating selected potential bioagent particles from said air;

a wetted wall sample preparer for preparing a sample of said selected potential bioagent particles, said wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector wherein said wetted wall sample preparer includes a wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid and a unit for adding optically encoded microbeads imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen to said liquid and said selected potential bioagent particles; and

a detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads and

wherein said detector includes a flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents.

2. The apparatus of claim 1 wherein said collector is an aerosol collector.

3. The apparatus of claim 1 wherein said air includes other particles in addition to said potential bioagent particles and wherein said collector includes a

separator for separating said potential bioagent particles from said other particles.

4. The apparatus of claim 3 wherein said potential bioagent particles are of a predetermined size range and said separator separates said potential bioagent particles are of a predetermined size range from said other particles.

5. The apparatus of claim 4 wherein said collector is an aerosol collector that collects air and includes means for separating said air into a bypass air flow that does not contain said potential bioagent particles of a predetermined particle size range and a product air flow that contains said potential bioagent particles of a predetermined particle size range.

12. The apparatus of claim 1 wherein said potential bioagent particles contain spores and including means for lysis of said spores.

15. The apparatus of claim 1 wherein said wetted wall sample preparer includes a sequential injection analysis system.

16. The apparatus of claim 1 wherein said wetted wall sample preparer includes a flow injection analysis system.

19. The apparatus of claim 1 wherein said wetted wall sample preparer includes a super serpentine reactor.

27. The apparatus of claim 1 wherein said optically encoded microbeads are polystyrene beads.

29. The apparatus of claim 1 wherein said flow cytometer for analyzing said optically encoded microbeads with said laser unit includes a red laser that classifies said microbeads and a green laser that quantifies said microbeads.

31. The apparatus of claim 1 wherein said detector includes a liquid-array based multiplex immunoassay detector.

32. The apparatus of claim 1 wherein said detector includes a multiplex PCR detector.

33. The apparatus of claim 1 including confirmation means for confirming said bioagents in said sample.

34. The apparatus of claim 33 wherein said confirmation means is a multiplex immunoassay detector.

35. The apparatus of claim 33 wherein said confirmation means is a multiplex PCR detector.

36. The apparatus of claim 33 wherein said confirmation means is a real time PCR detector.

37. The apparatus of claim 33 wherein said confirmation means includes means for performing PCR amplification.

38. The apparatus of claim 33 wherein said confirmation means includes means for injecting/aspirating a sample, means for adding PCR reagent, means for mixing sample and reagent, means for transport to PCR reactor, means for performing PCR amplification, means for transport of amplified sample from PCR reactor, and means for detection of PCR amplicon.

39. The apparatus of claim 33 wherein said confirmation means includes means for injecting/aspirating a sample, means for adding PCR reagent, means for mixing sample and reagent, means for transport to PCR reactor, means for performing PCR amplification, means for transport of amplified sample from PCR reactor, means for detection of PCR amplicon, and means for decontamination and conditioning of all exposed conduits.

40. The apparatus of claim 1 wherein said sample preparation means includes optically encoded microbeads and bead suspension/mixer means for suspending said microbeads for a predetermined time period.

IX. EVIDENCE APPENDIX

There are no entries in the Evidence Appendix.

X. RELATED PROCEEDINGS APPENDIX

There are no entries in the Related Proceedings Appendix.